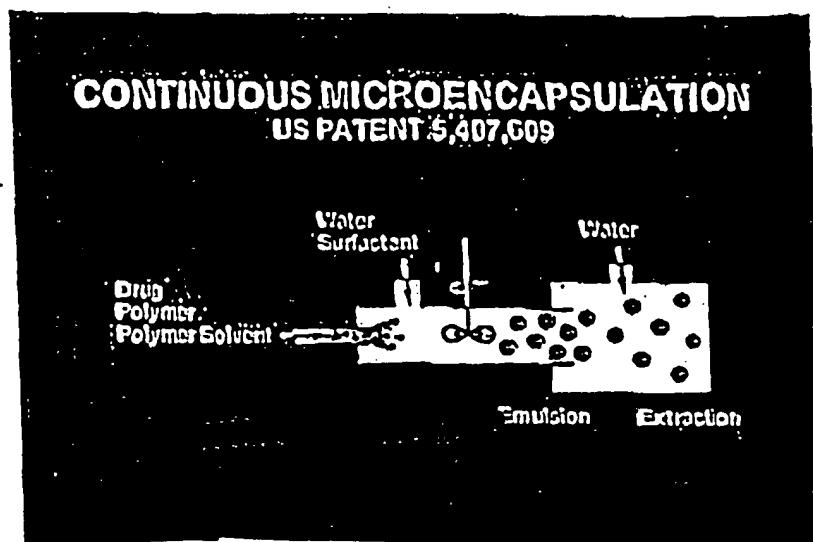




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SOUTHERN RESEARCH'S PATENTED MICROENCAPSULATION PROCESS



Advantages

- US Patent issued 1995
- Fast encapsulation time ~ milliseconds
- Minimal exposure to polymer solvent
- High encapsulation efficiency
- Good Yields
- Makes small microparticles
<100 micron <10 micron

Drugs Microencapsulated

- Proteins
- Peptides
- Small molecules
- Water-soluble drugs
- Hydrophobic drugs
- Drugs encapsulated in lactide/glycolide polymers

FIGURE 1

FIGURE 2

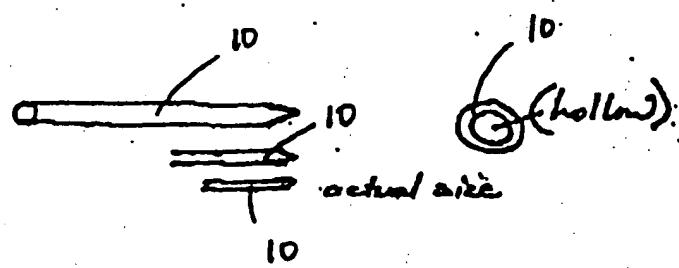


FIGURE 3

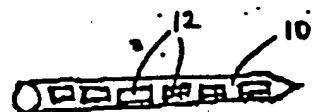
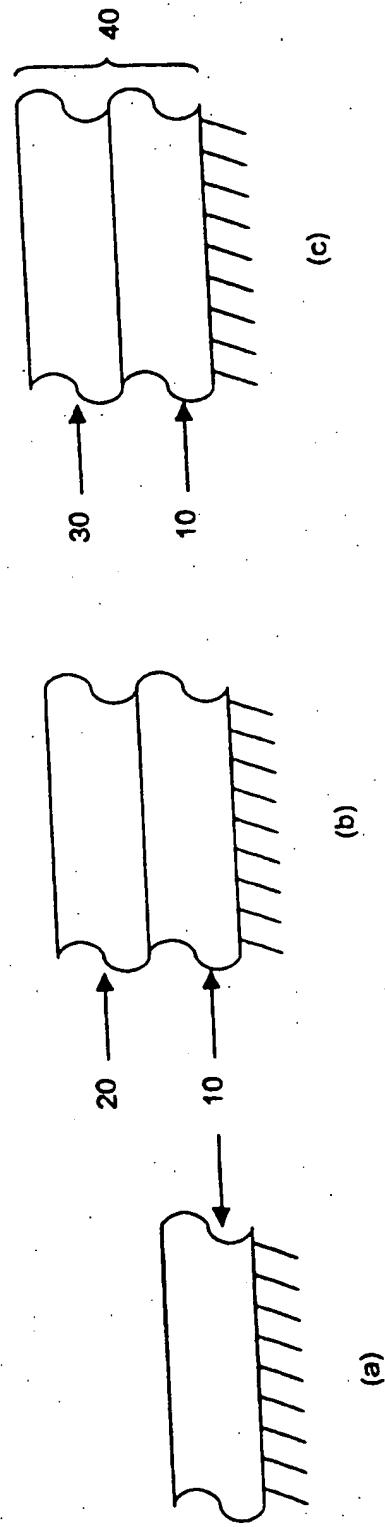


FIGURE 4



Conditions: Ambient				
Material:	PX510	PX261	PX749	PX125
Hardness:	F	B	3B	4B

Conditions: 5 minutes in 37°C pH 7.4 Saline Buffer				
Material:	PX510	PX261	PX749	PX125
Hardness:	F	B	9B	<9B

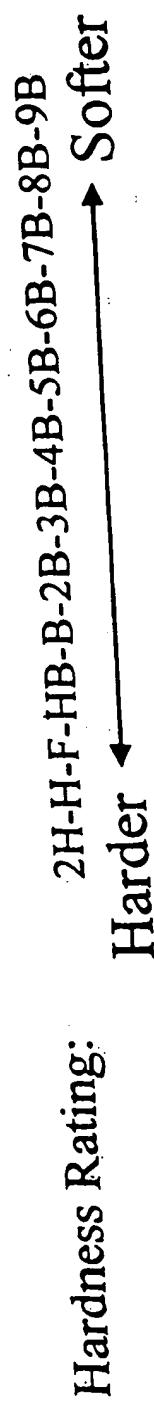


FIGURE 5

Conditions: Ambient

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Resistance To Cracking	< 3 mm				

Conditions: 5 minutes in 37°C pH 7.4 Saline Buffer

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Resistance To Cracking	< 3 mm				

FIGURE 6

Conditions: Ambient

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Class:	5B	5B	5B	4B	5B

Class Rating: 5B = 0% of coating removed from substrate
4B = Less than 5% of coating removed from substrate

FIGURE 7

FIGURE 8

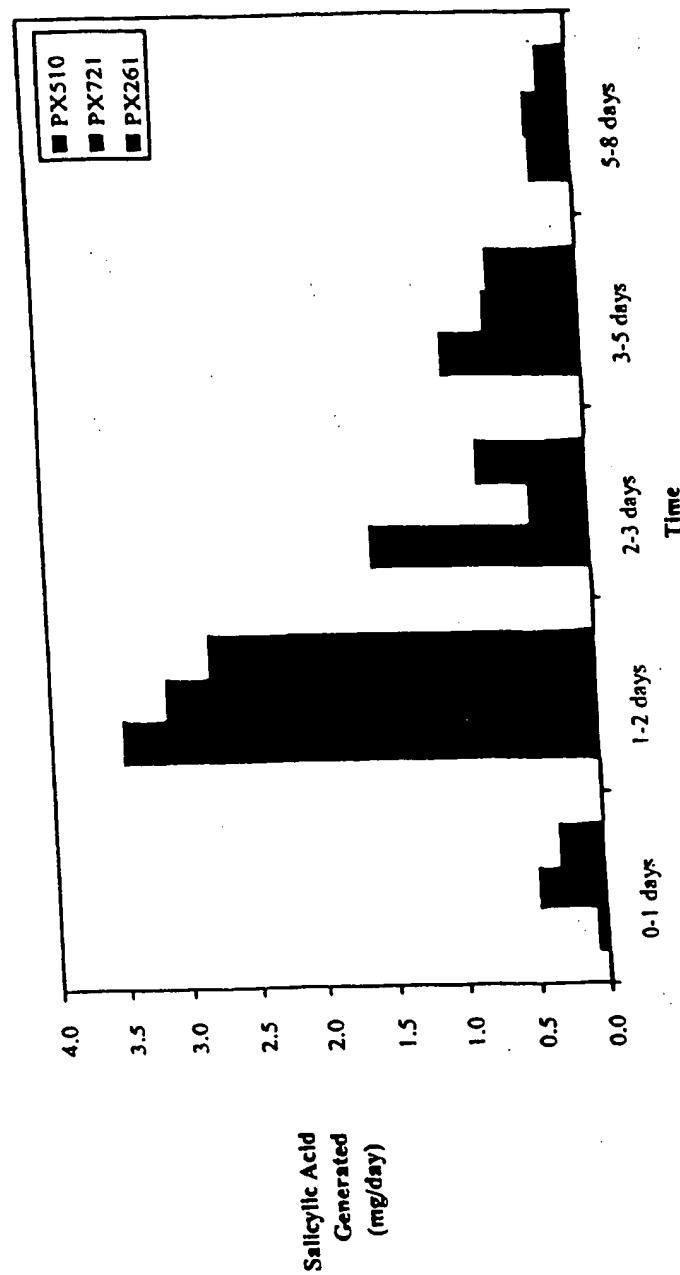


FIGURE 8B

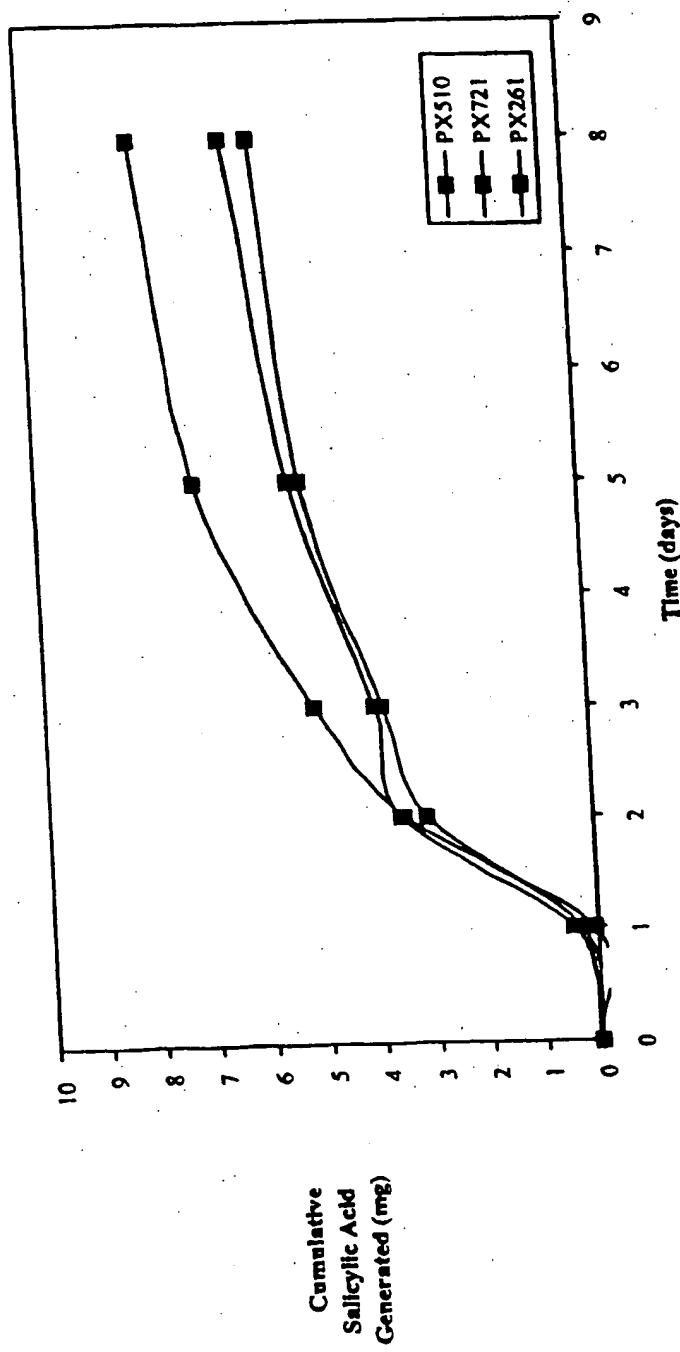


FIGURE 9A

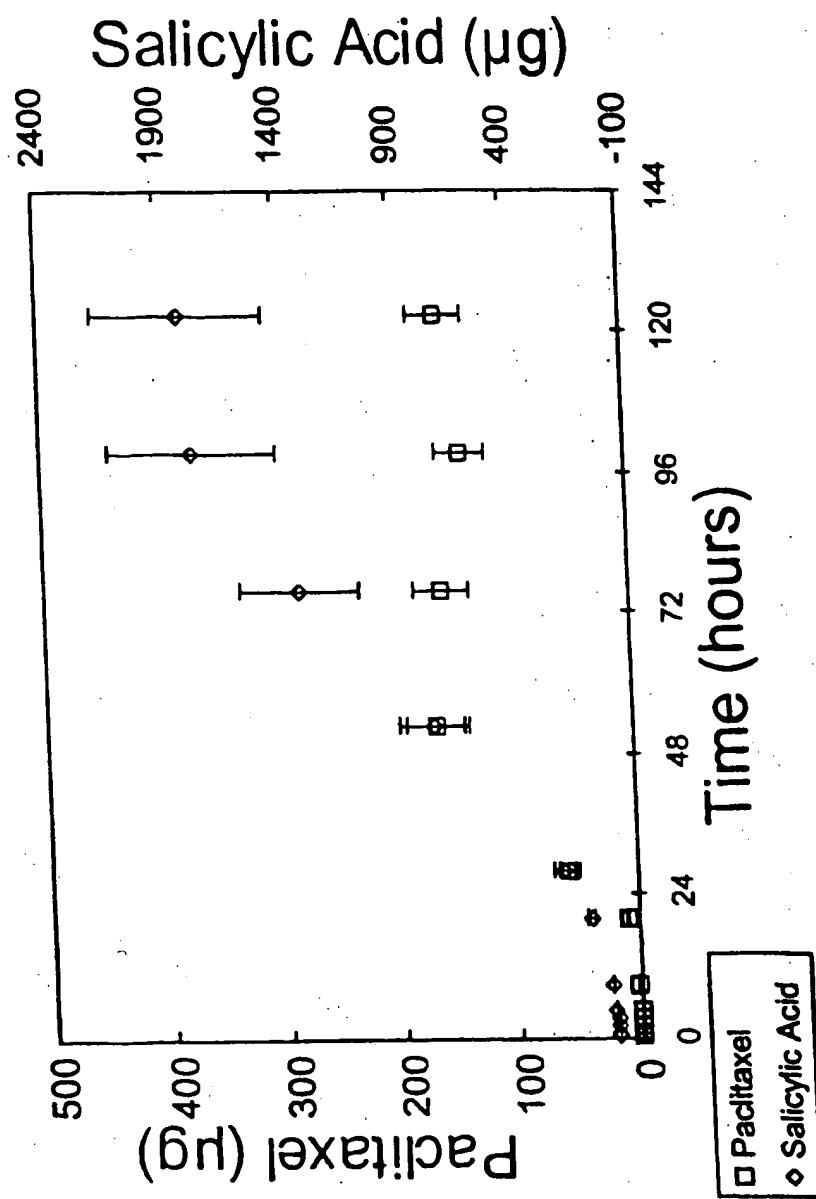
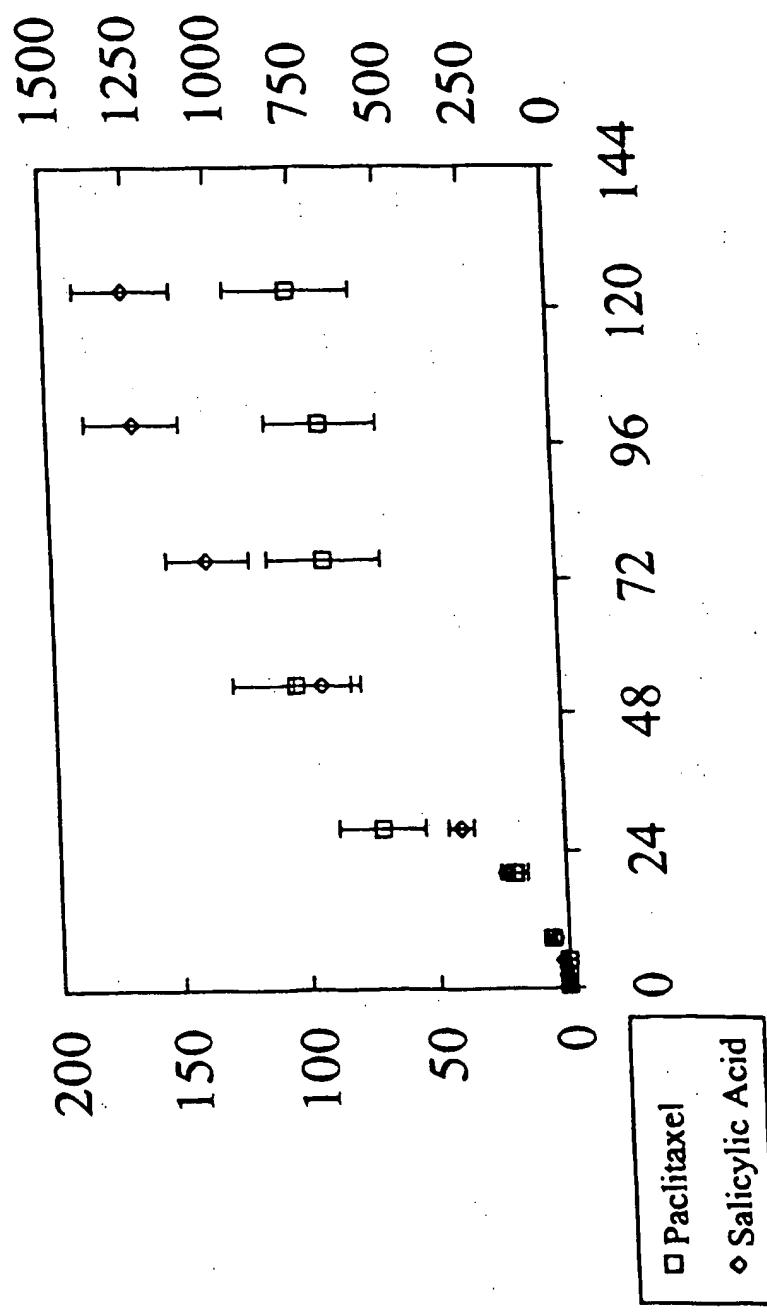


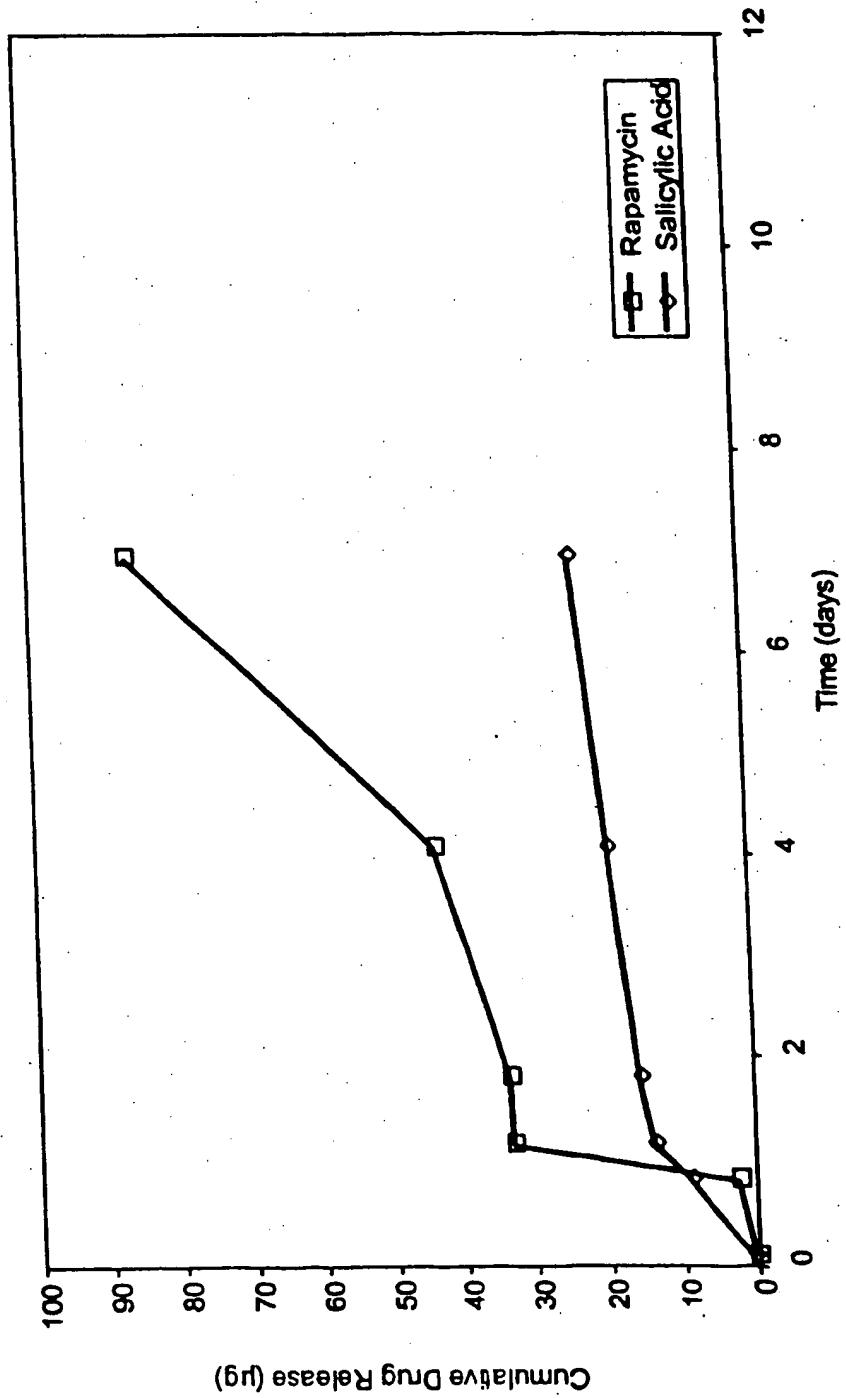
FIGURE 9B



Property	PX510	PX721	PX261	PX749
T _g (C)	44	38	29	16
Tensile modulus (MPa)	2.0 (25 C) 5.1 (37 C)			3.0 (25 C)
Yield Strength (MPa)		Not observed		6.0 (25 C)
Ultimate Elongation (%)		1.5 (25 C) 350 (37 C)		500 (25 C)

FIGURE 10

FIGURE 11



	E Beam (3 MRad)			γ (25-35 KGyrs)		
Property	PX510	PX721	PX261	PX510	PX721	PX261
MW	-28%	-39%	-26%	-14%	N/C	N/C
Hardness	-2 units	N/C	-1 unit	N/C	-3 units	-2 units
Flexibility	N/C	N/C	N/C	N/C	N/C	N/C
Adhesion	N/C	N/C	-1 unit	N/C	N/C	N/C
				N/C: no change		

FIGURE 12

FIGURE 13A

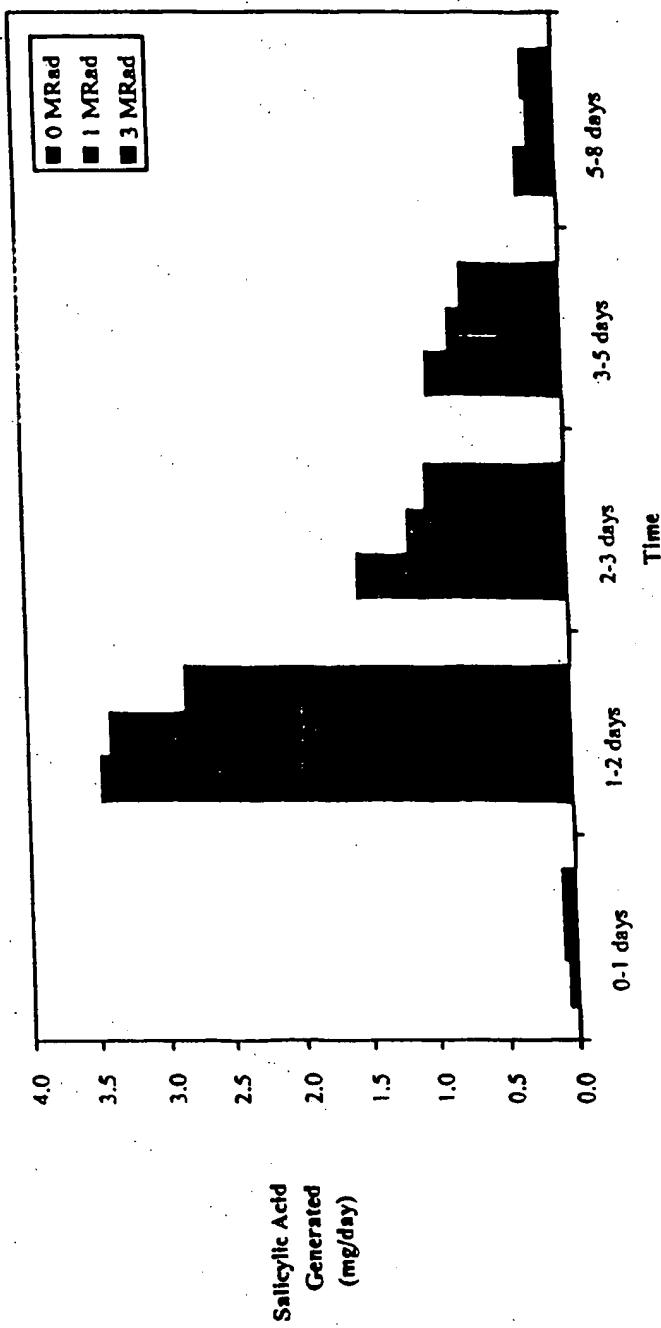
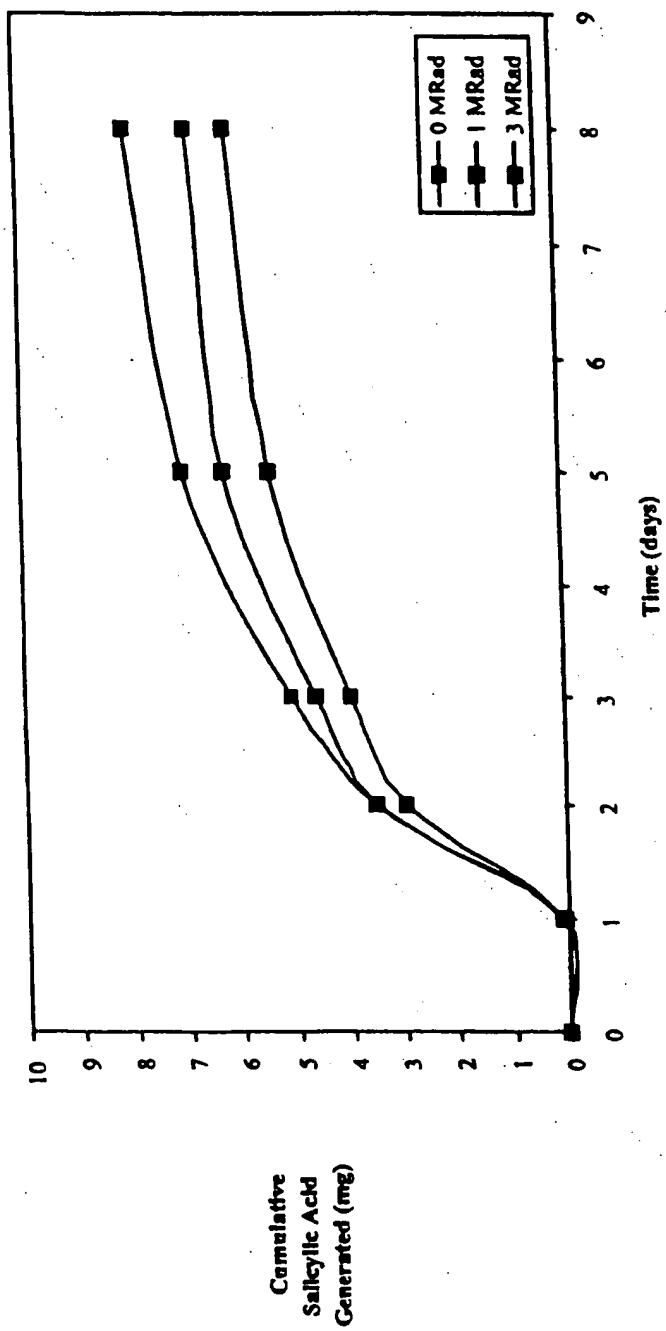


FIGURE 13B



PX242 20-53 Coated Coupon Diflunisal Elution

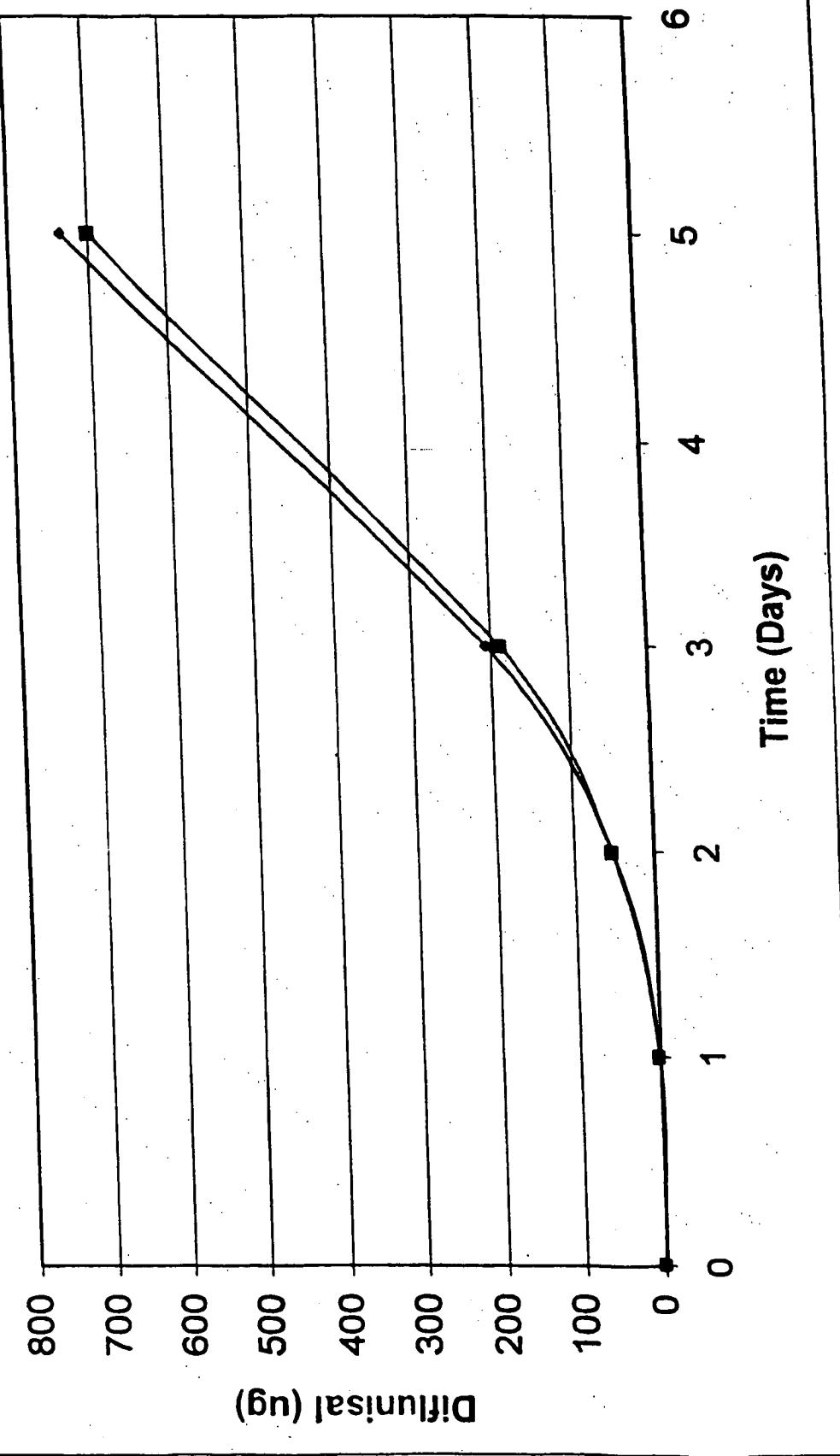


FIGURE 14

PX242 20-53 Coated Coupon Diffunisal Elution

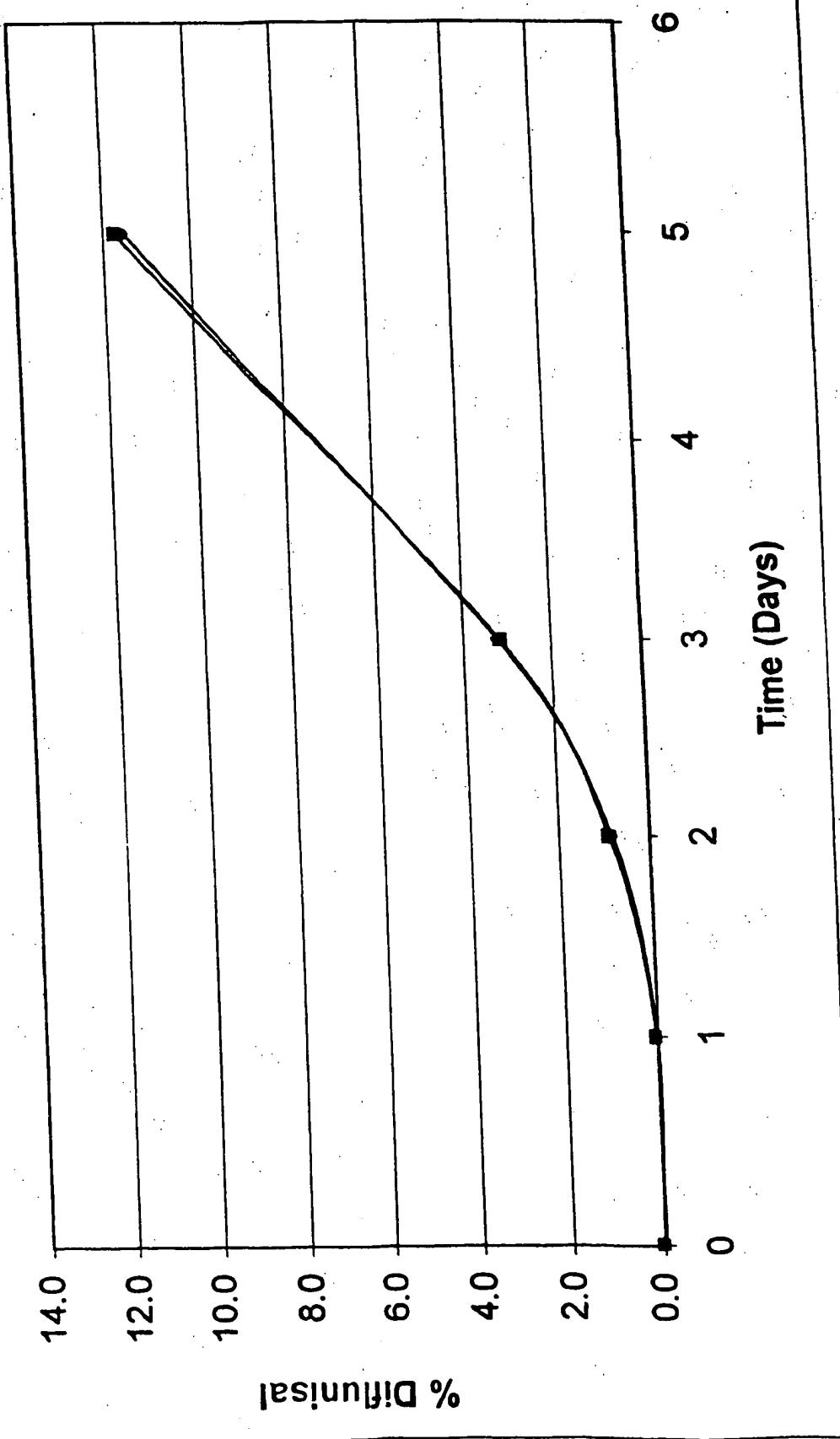
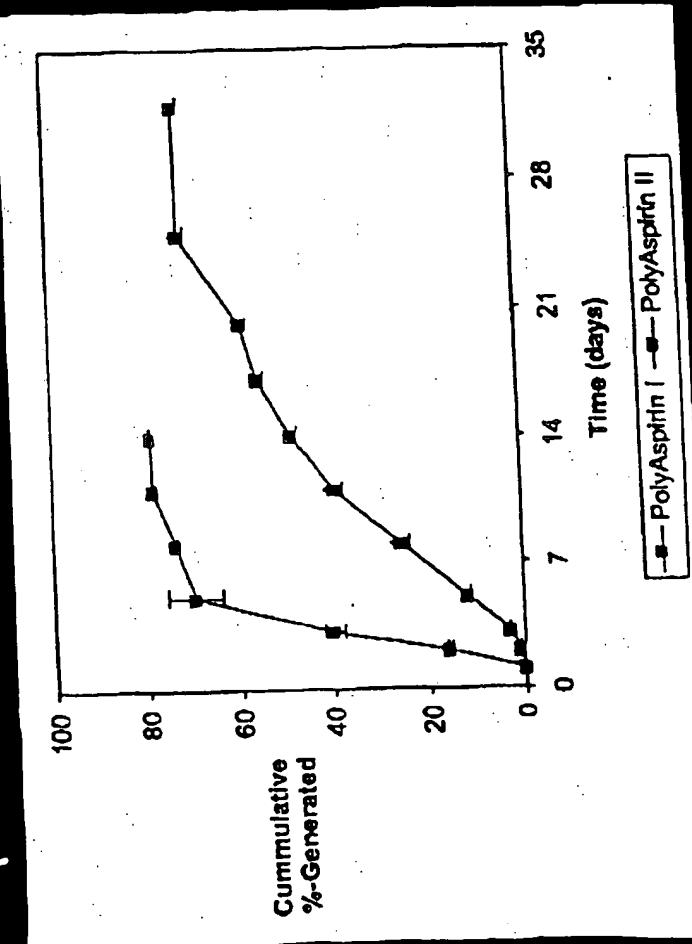


FIGURE 15

Erosion of PolyAspirin I & II

Generation of NSAID into 37 °C pH 7.4 PBS from ~5 μm -thick Coatings on 316L SS Plates



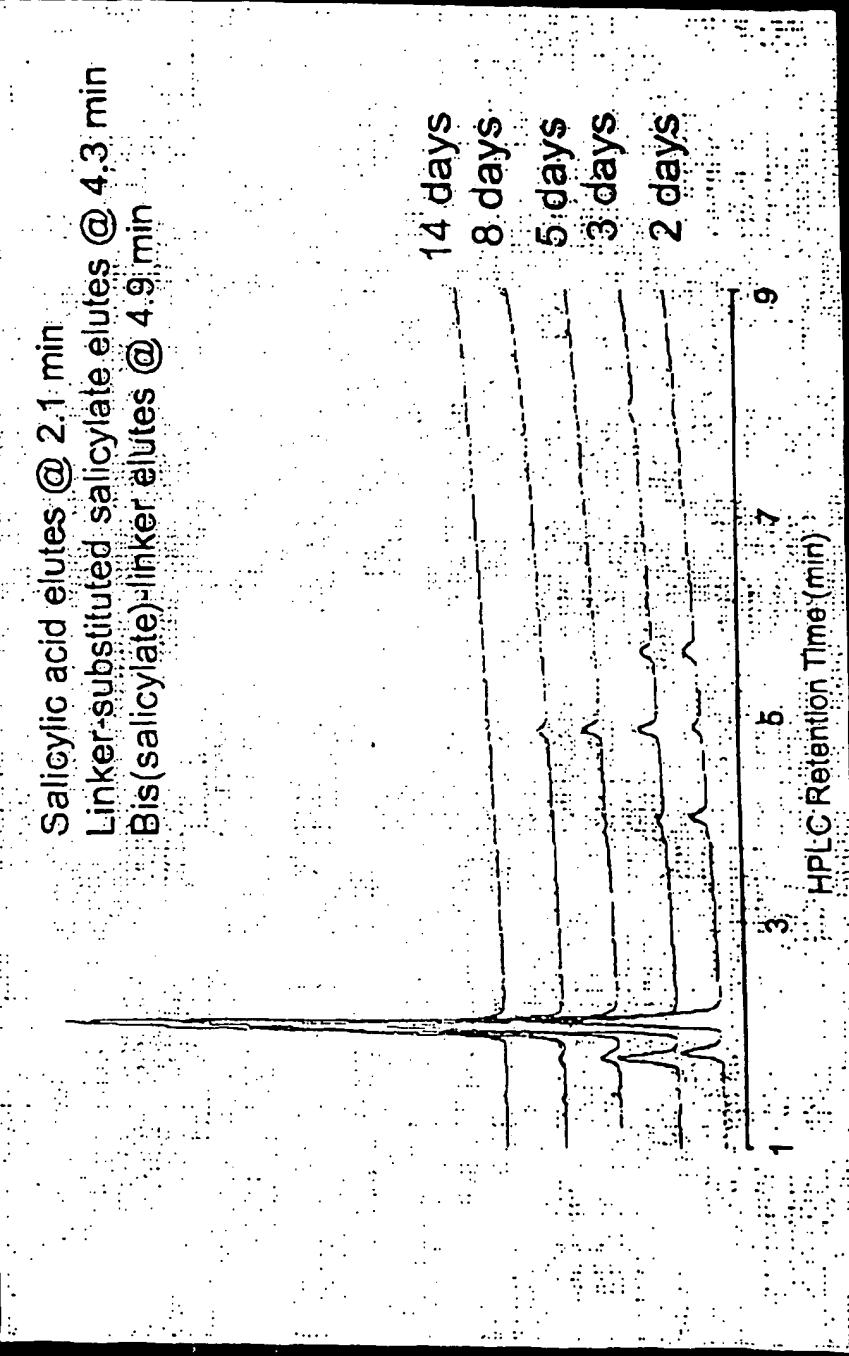
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FIGURE 16

Erosion Profile for PolyAspirin I

Salicylic acid elutes @ 2.1 min
Linker-substituted salicylate elutes @ 4.3 min
Bis(salicylate)-linker elutes @ 4.9 min

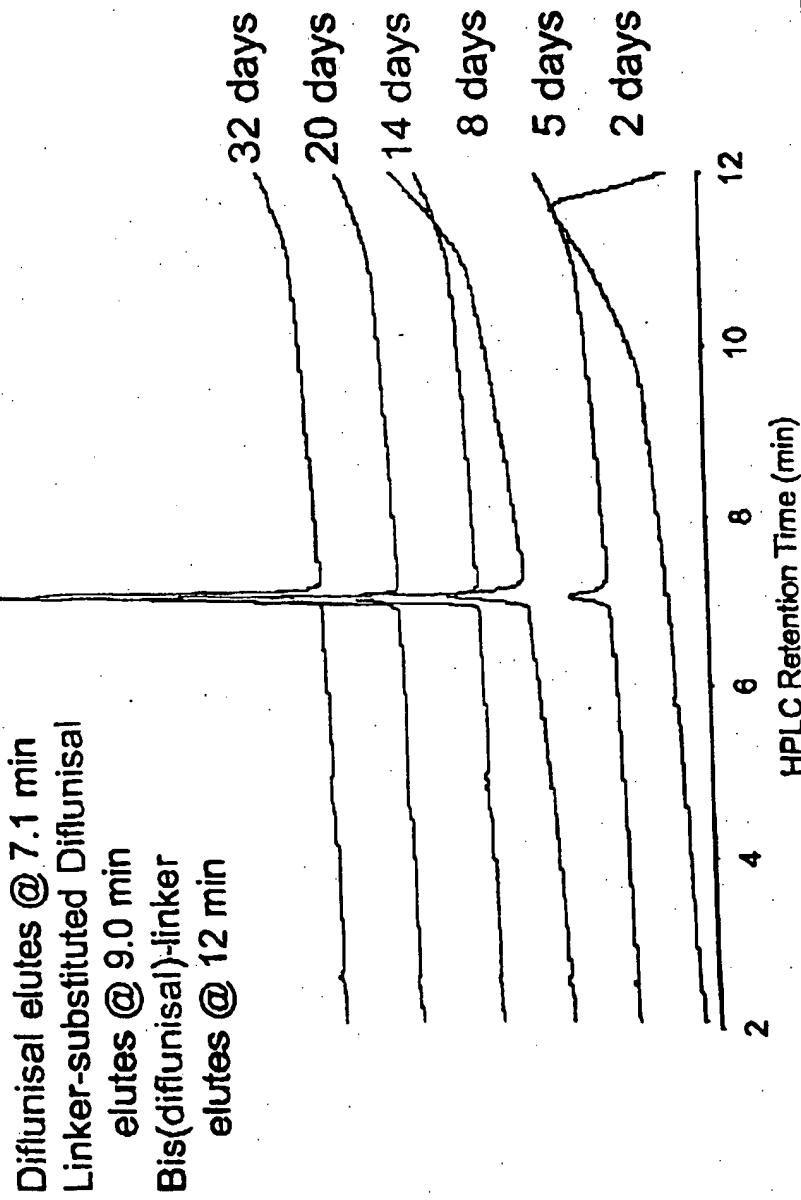


component

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FIGURE 17

Erosion Profile for PolyAspirin II



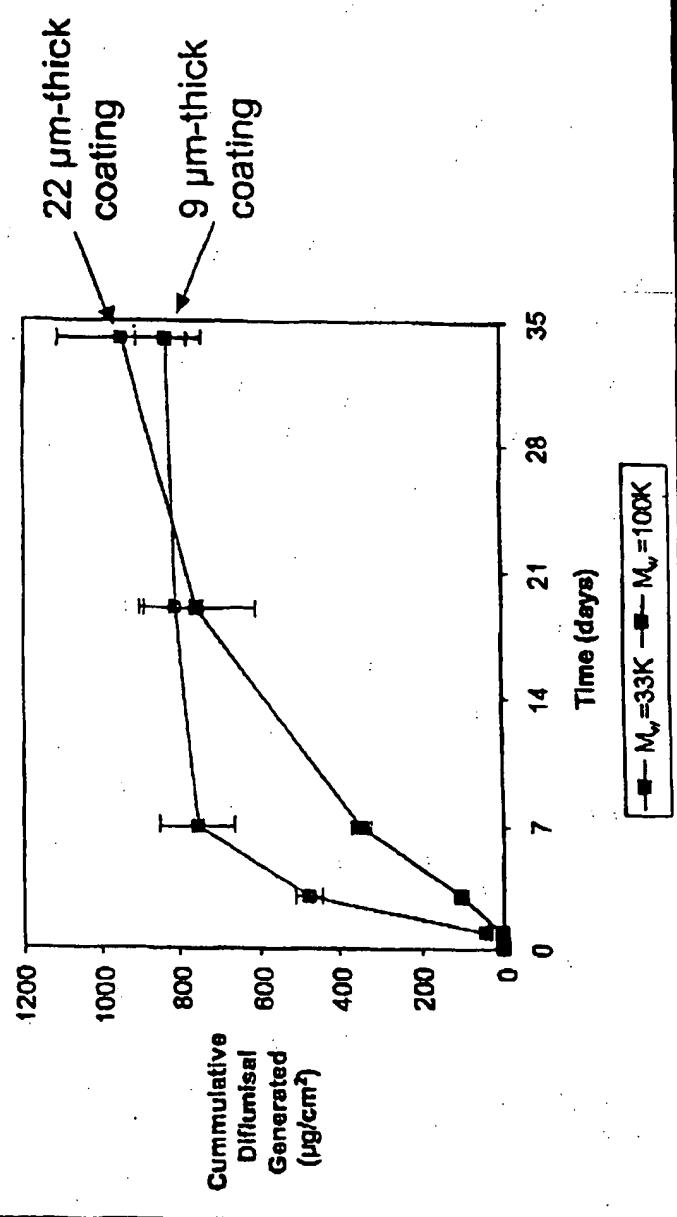
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FIGURE 18

Effect Of MW On Erosion

Generation of Diflunisal from PolyAspirin II into 37 °C Serum from Coatings on 316L SS Plates

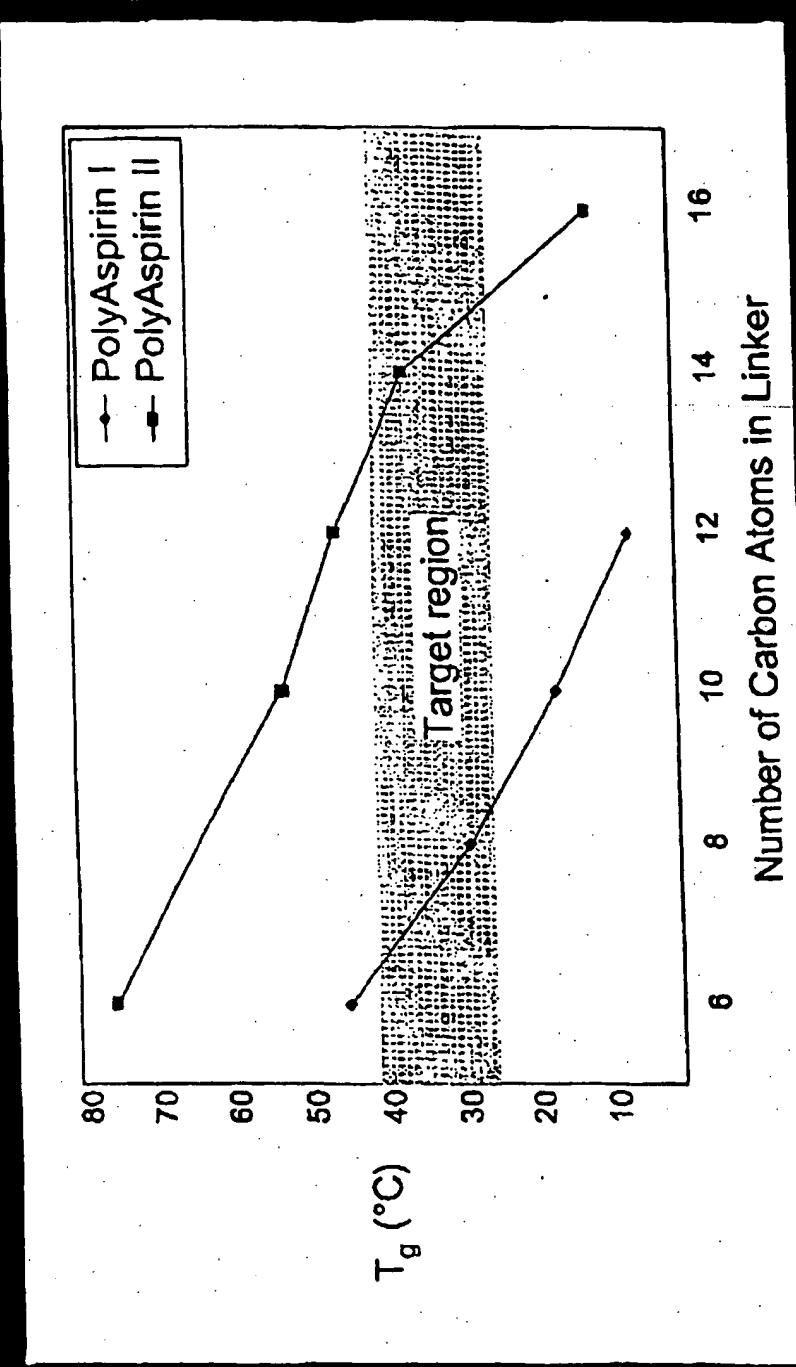


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FIGURE 19

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Tuning Mechanical Properties



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FIGURE 20

Thermoanalysis of PolyAspirin™

Property	PolyAspirin I		PolyAspirin II	
	PX261 $M_w \sim 20K$	PX657 $M_w \sim 33K$	PX657 $M_w \sim 100K$	
T_g (°C)	29	36	44	
Ultimate Stress (kPa)	>1700 (25°C) >2000 (37°C)	>2800 (25°C)	>2600 (25°C)	
Ultimate Elongation (%)	>500 (25°C) >500 (37°C)	>4 (25°C)	>500 (25°C)	
Toughness (kPa)	>3900 (25°C) >4400 (37°C)	>560 (25°C)	>4000 (25°C)	

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FIGURE 21

Properties of PolyAspirin™ Coatings

PolyAspirin I

PX261
 $M_w \sim 20K$

Test

Hardness

Ambient
5 min in PBS, 37 °C
1 hr in PBS, 37 °C

B B .

3H
B
4B

F 2B
8B

PolyAspirin II

PX657

$M_w \sim 33K$ $M_v \sim 100K$

Flexibility

Ambient
5 min in PBS, 37 °C
1 hr in PBS, 37 °C

<3 mm
<3 mm
<3 mm

<3 mm
<3 mm
<3 mm

<3 mm
<3 mm
<3 mm

Adhesion

Ambient
5B

5B

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FIGURE 22

PolyAspirin Coatings with Admixtures

PolyAspirin II (PX657)
20% Pectin/Taxel Admixed

Test	No Admixture	20% Pectin/Taxel Admixed
<u>Hardness</u>		
Ambient		
5 min in PBS, 37 °C	F	F
1 hr in PBS, 37 °C	2B	6B
<u>Flexibility</u>		
Ambient		
5 min in PBS, 37 °C	<3 mm	<3 mm
1 hr in PBS, 37 °C	<3 mm	<3 mm
<u>Adhesion</u>		
Ambient		
	5B	5B

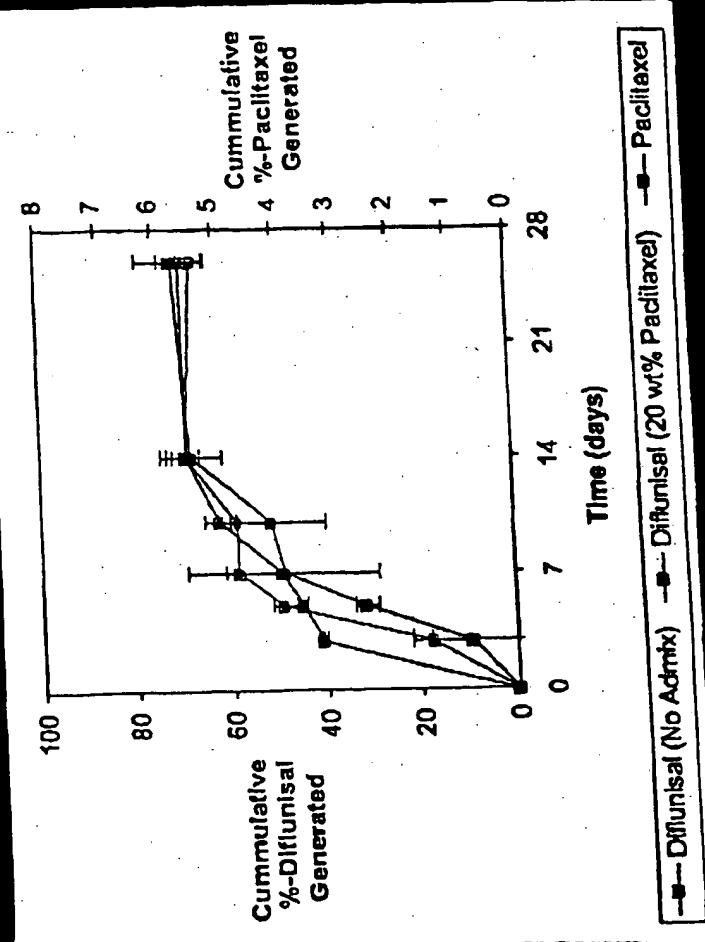
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FIGURE 23

Erosion Of PolyAspirin I & II

Diflunisal Generation & Paclitaxel Release into 37 °C Serum from ~5 μm-thick Coatings on 316L SS Plates



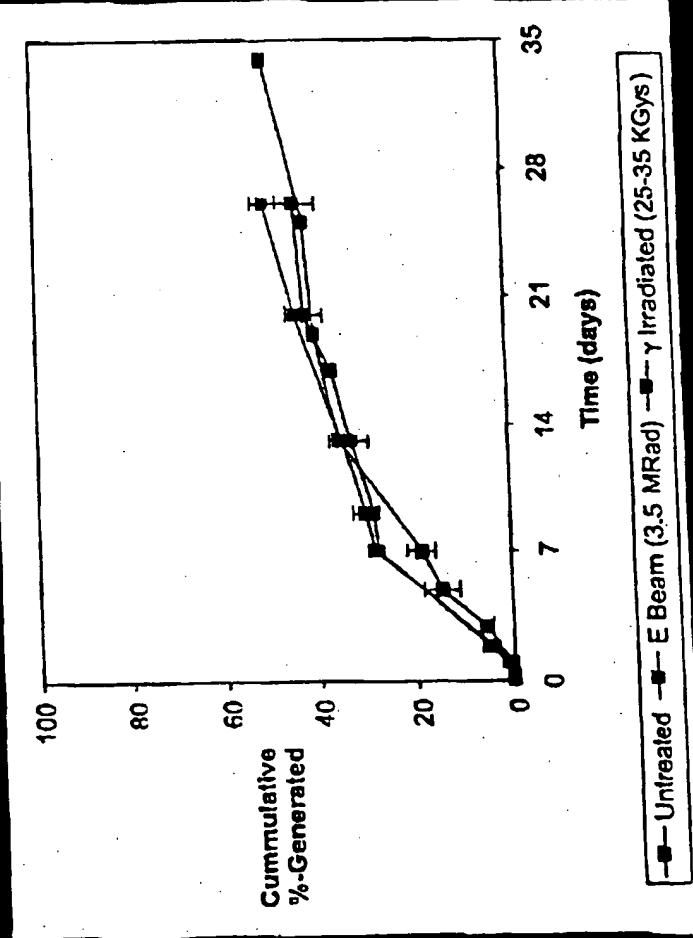
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FIGURE 24

Erosion of Sterilized PolyAspirin II

Generation of Diflunisal into 37 °C Serum from
~5 μm -thick Coatings on 316L SS Plates



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FIGURE 25

γ Irradiation (25-35 Kgy's)

Property	PolyAspirin I	PolyAspirin II
MW	PX281 $M_w \sim 20K$	PX657 $M_w \sim 100K$
Hardness	N/C	-50%
Flexibility	-2 units	-3 units
Adhesion	N/C	N/C: no change
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FIGURE 26

E Beam (3-4.5 Mrad)

PolyAspirin I

PolyAspirin II

Property	PX261 $M_w \sim 20K$	PX657 $M_w \sim 33K$	PX657 $M_w \sim 80K$
MW	-26%	+45%	-30%
Hardness	-1 unit	+2 units	N/C
Flexibility	N/C	-	N/C
Adhesion	-1 unit	-	N/C: no change
			CONFIDENTIAL

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FIGURE 27

Kinetics of NSAID Generation

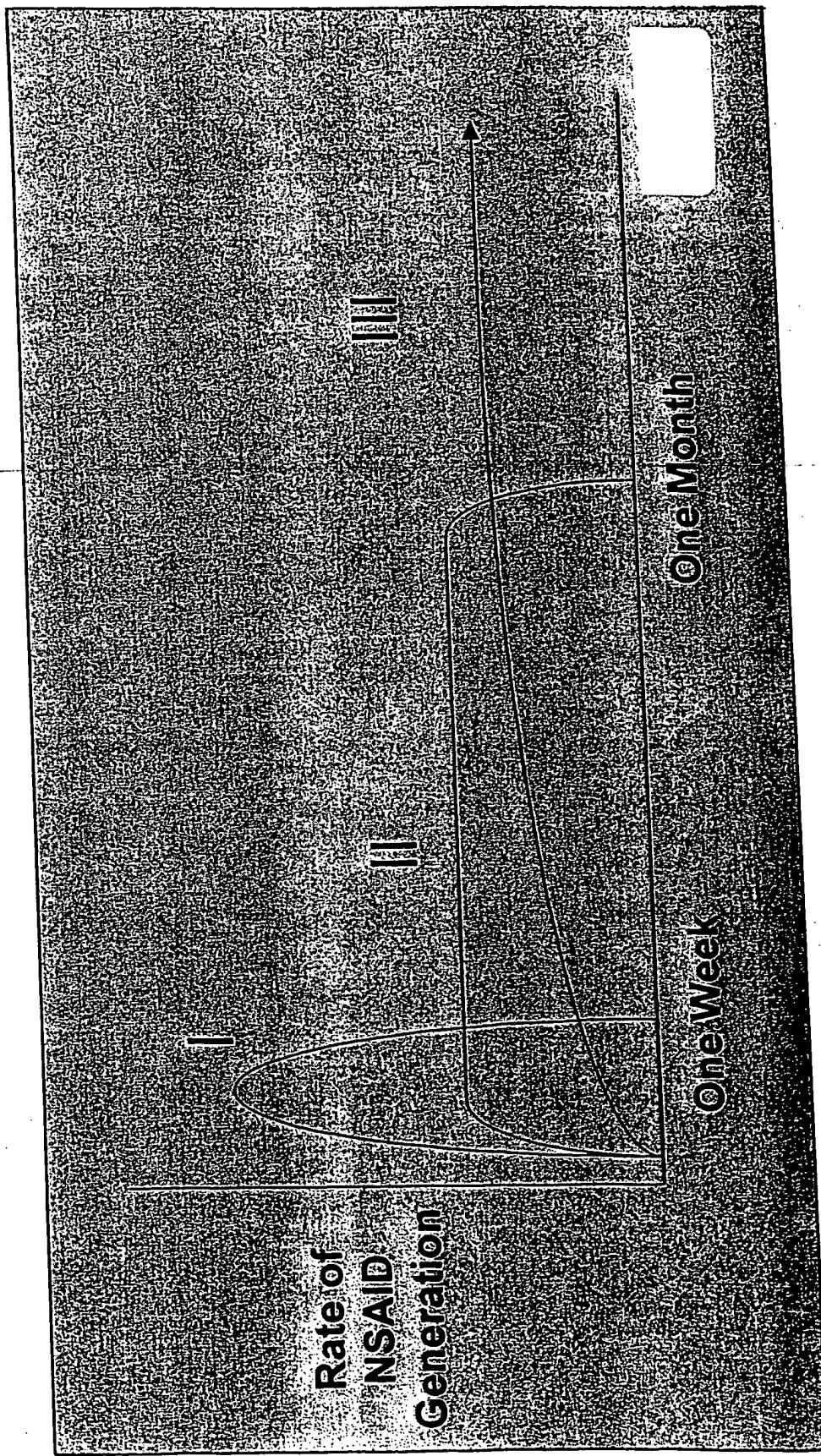


FIGURE 28

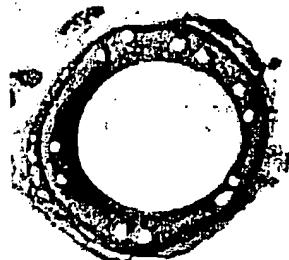


FIGURE 29

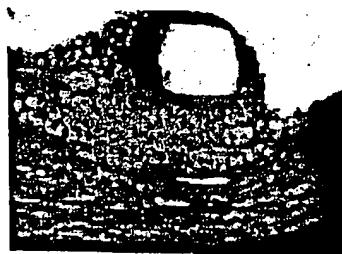
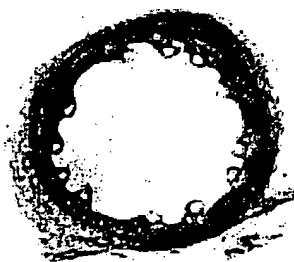


FIGURE 30

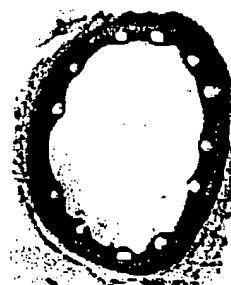


FIGURE 31

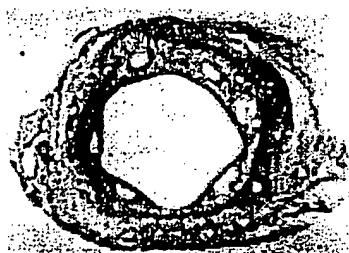


FIGURE 32



FIGURE 33



FIGURE 34

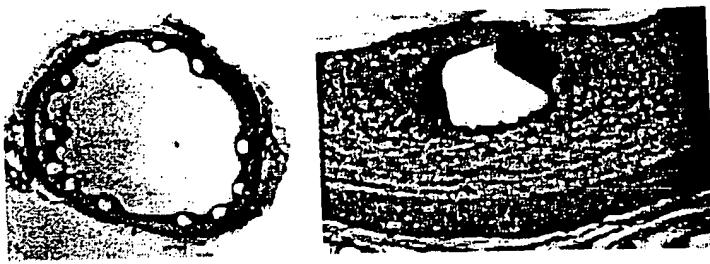


FIGURE 35

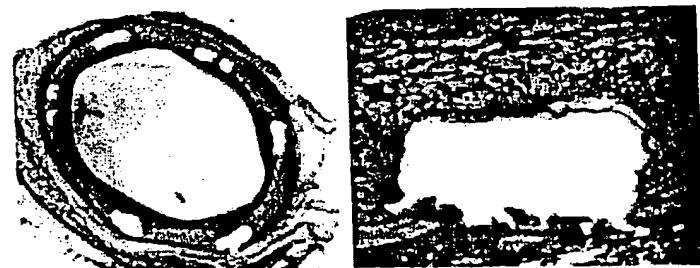
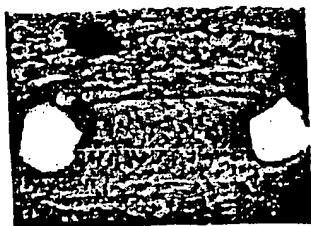


FIGURE 36

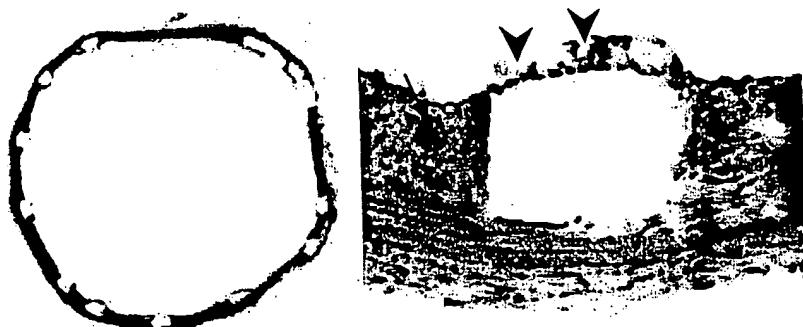
FIGURE 37



FIGURE 38



FIGURE 39



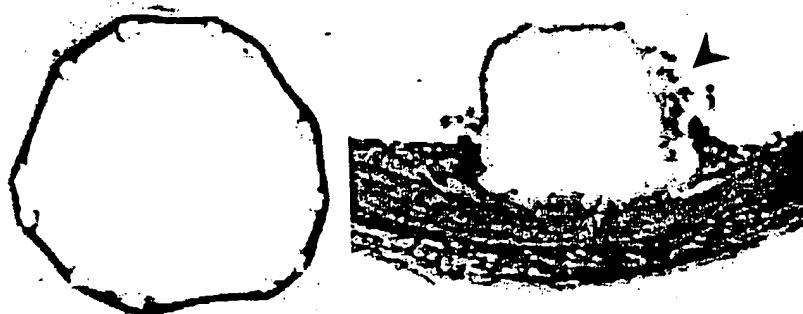


FIGURE 40

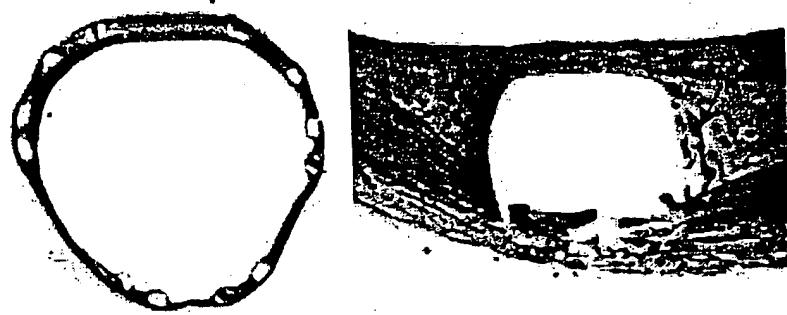


FIGURE 41

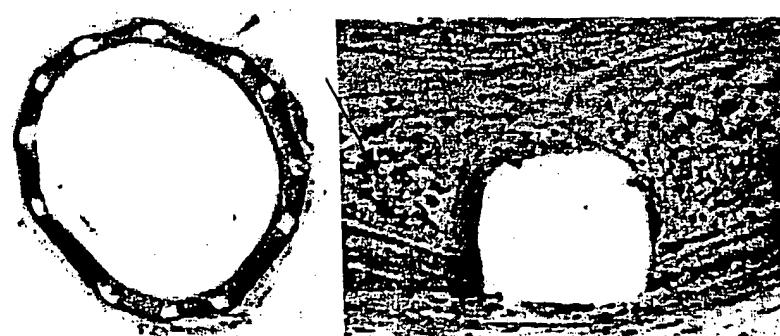


FIGURE 42

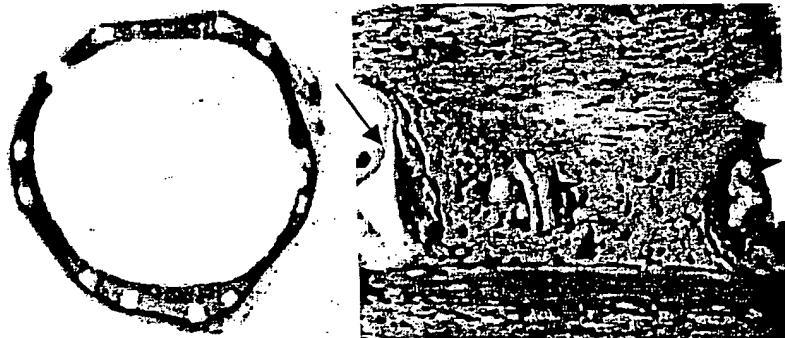


FIGURE 43

uncrimped/unexpanded

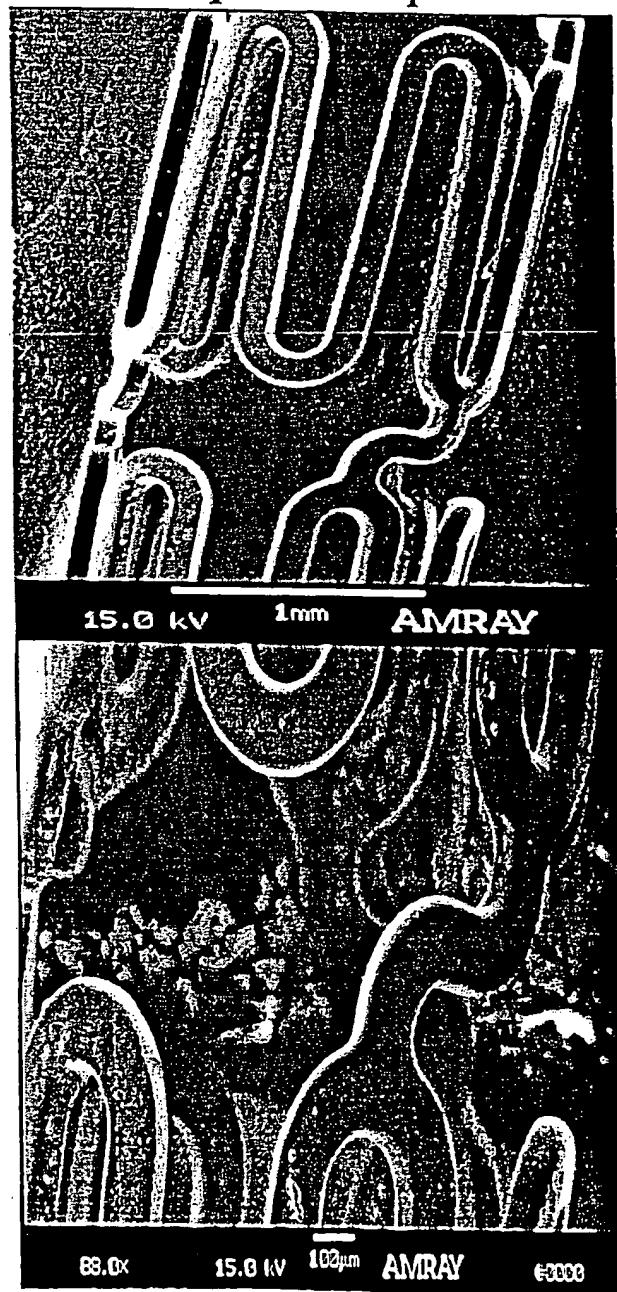


FIG. 44a

FIG. 44b

uncrimped/unexpanded

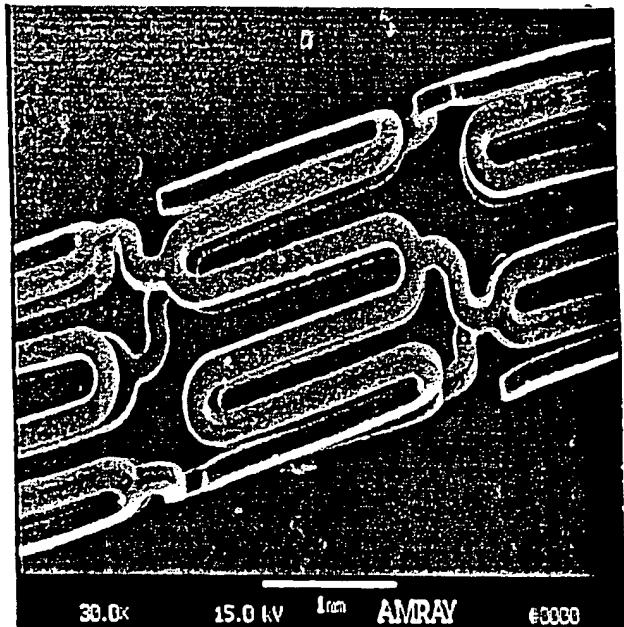


FIG. 45a

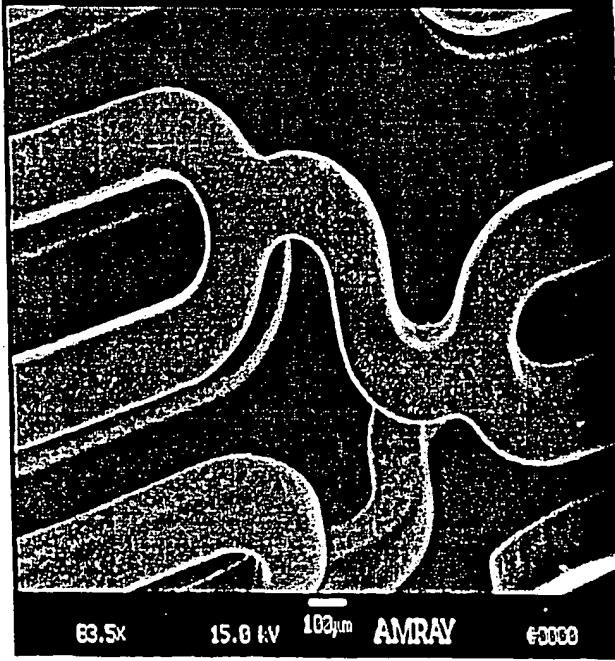


FIG. 45b

uncrimped/unexpanded

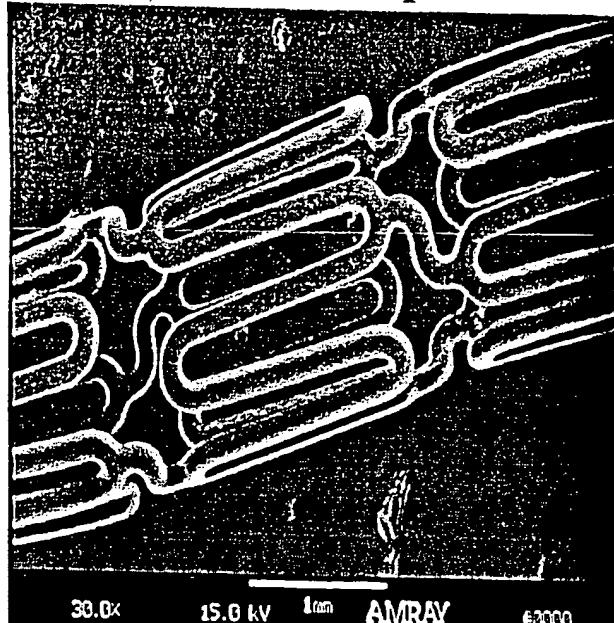


FIG. 46a

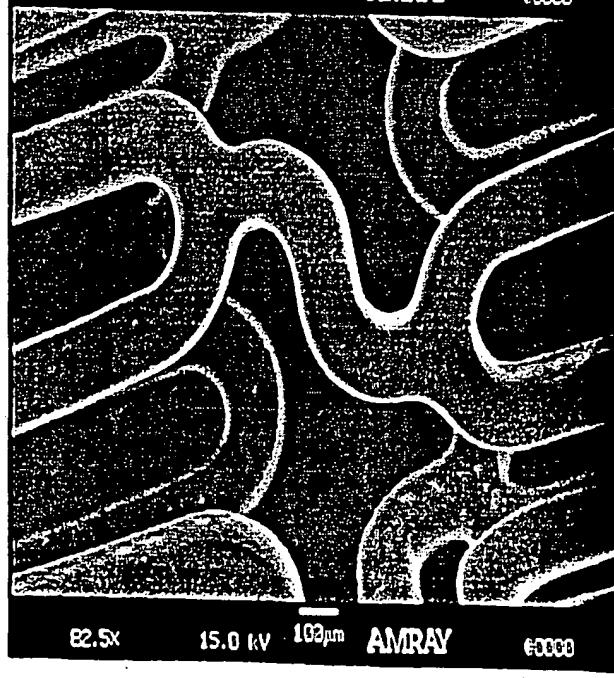


FIG. 46b

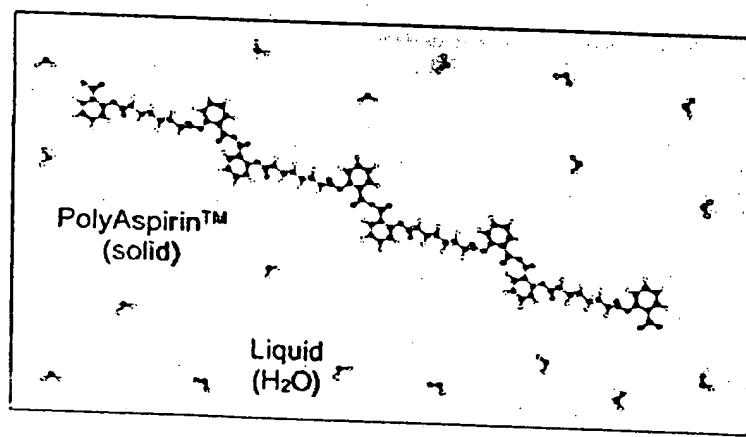


FIGURE 47



FIGURE 48

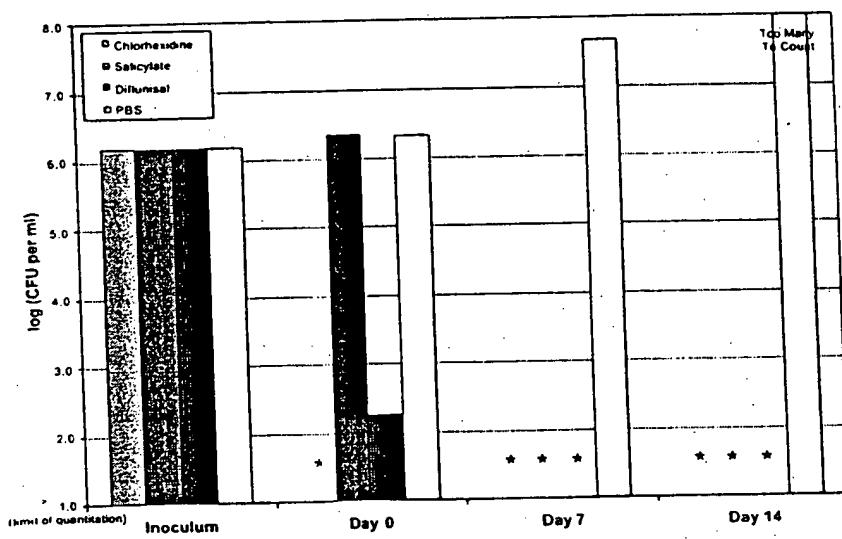


FIGURE 49

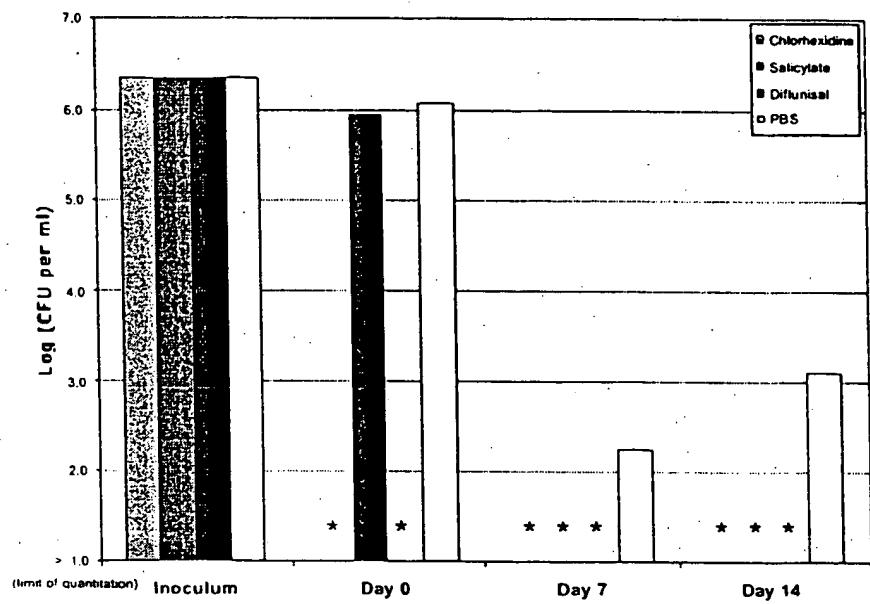


FIGURE 50

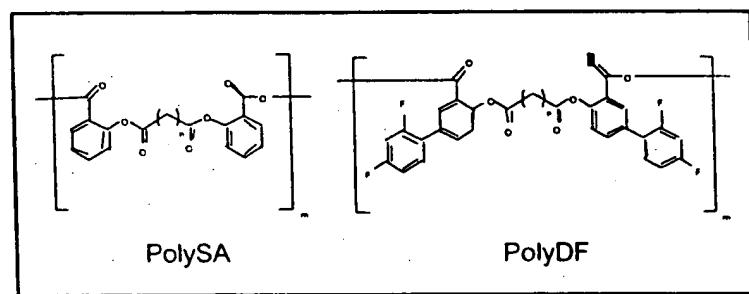


FIGURE 51

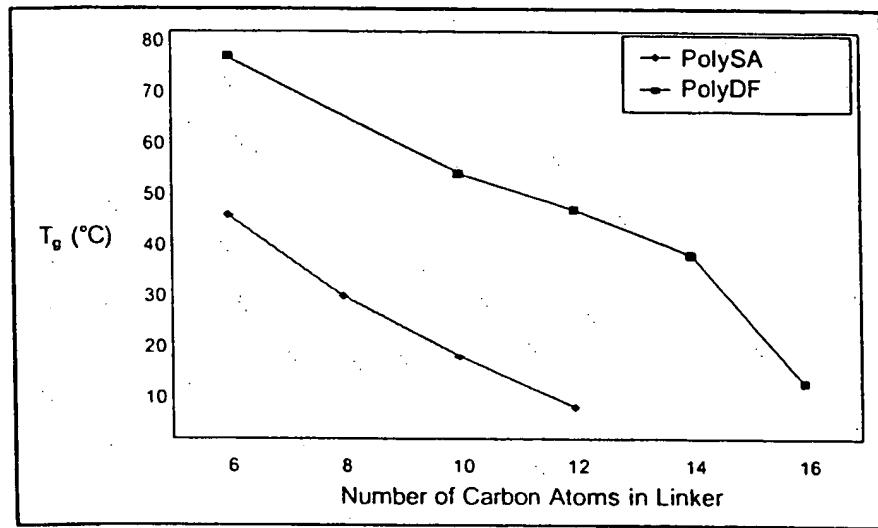


FIGURE 52

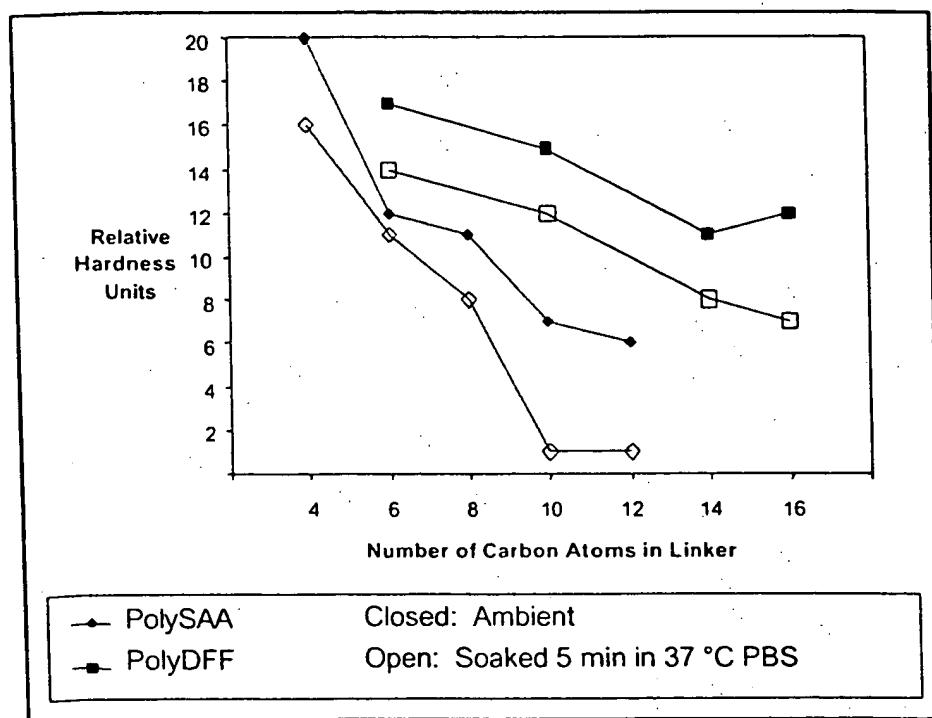


FIGURE 53

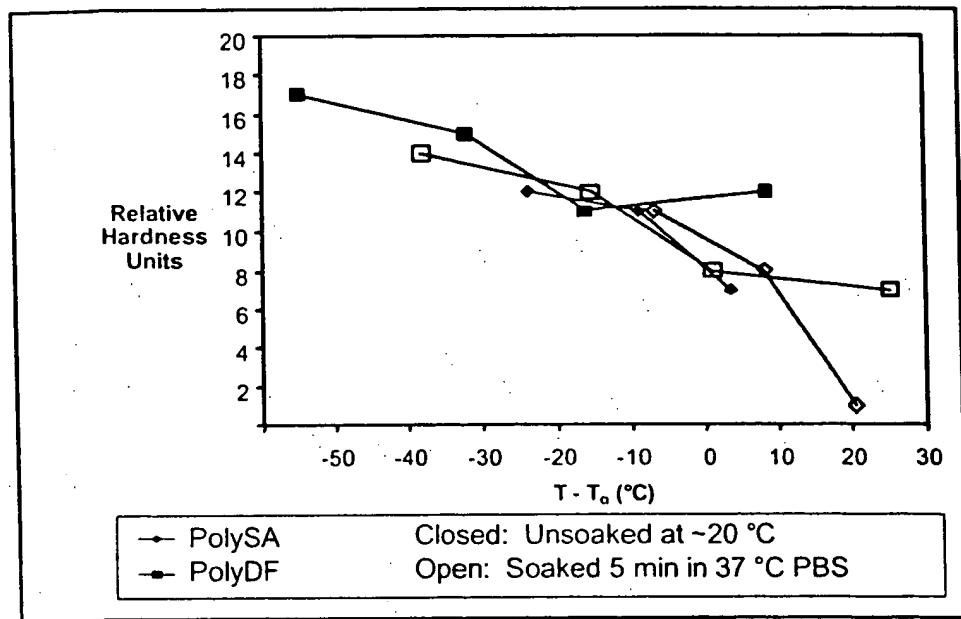


FIGURE 54

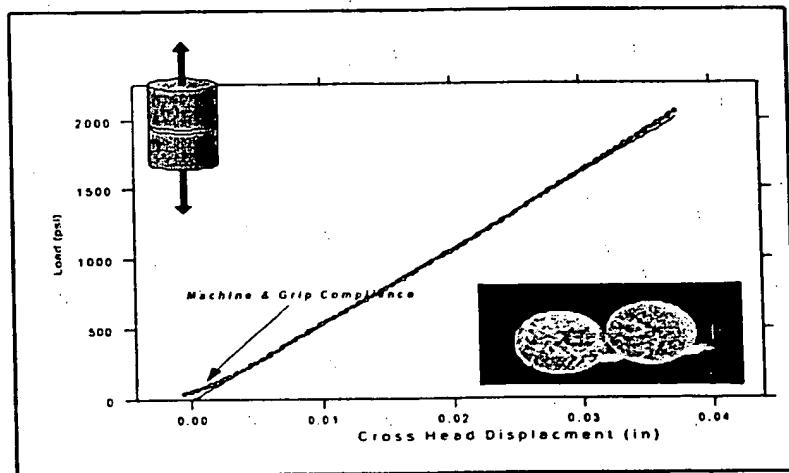


FIGURE 55

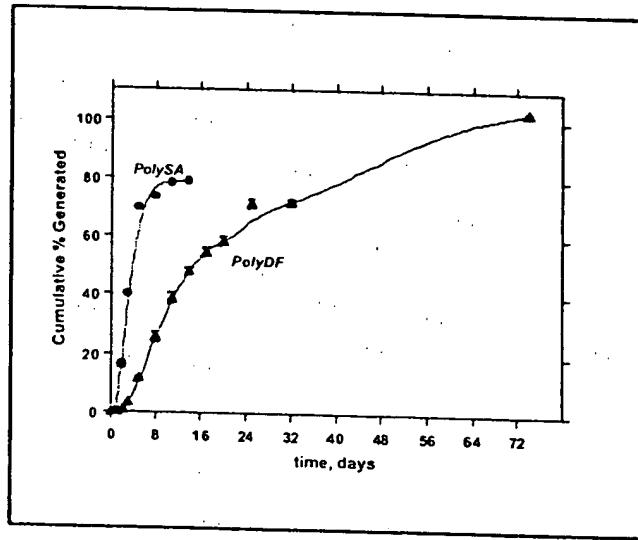


FIGURE 56

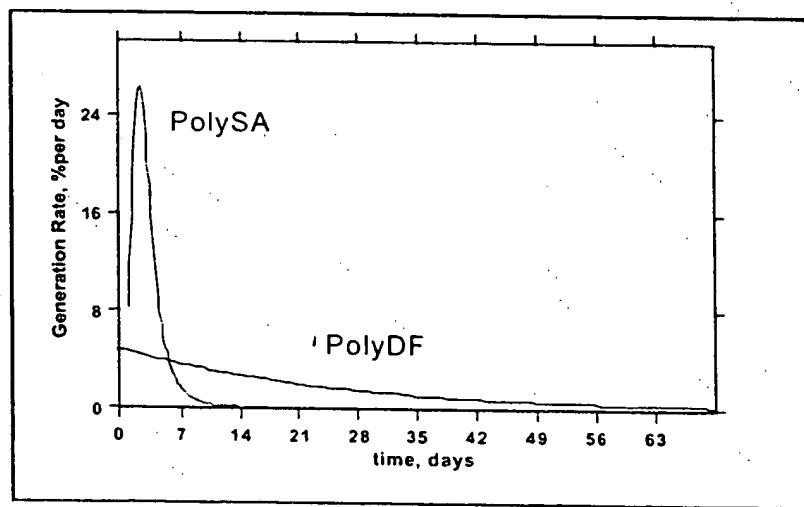


FIGURE 57

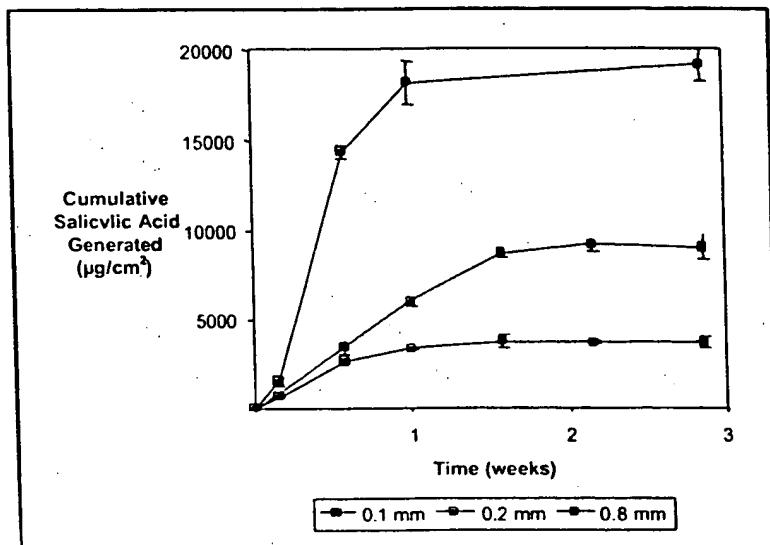


FIGURE 58

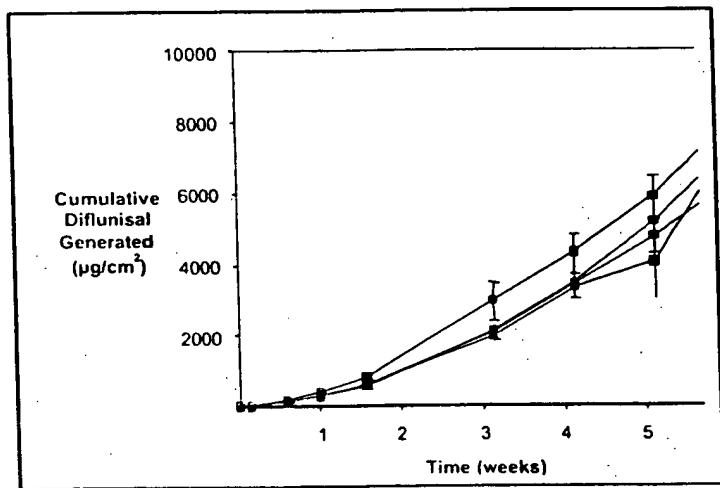


FIGURE 59

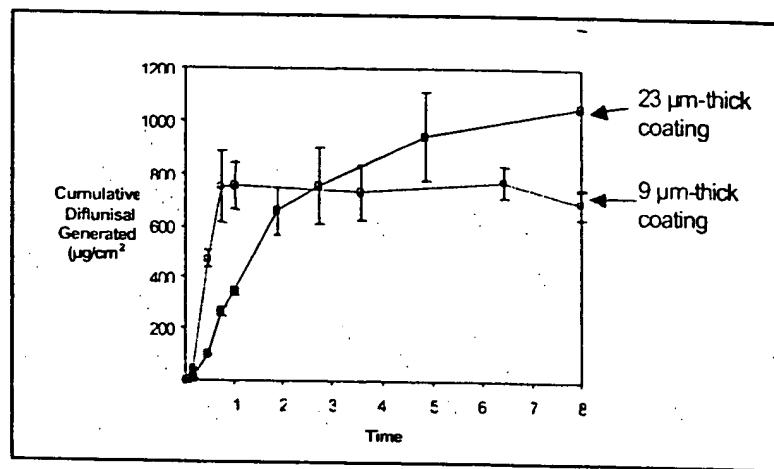


FIGURE 60

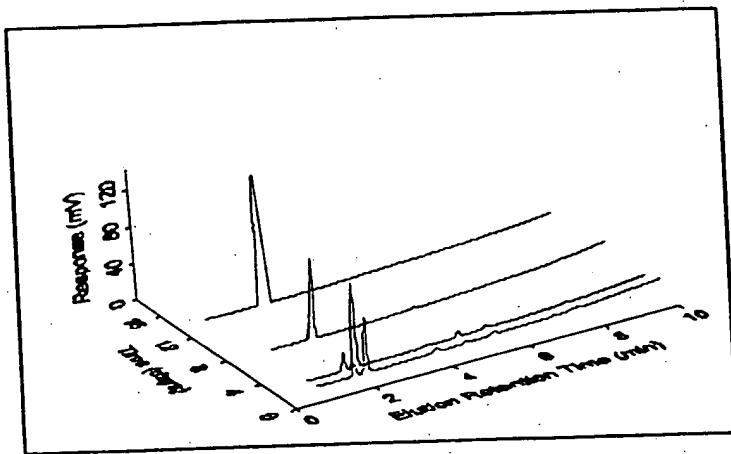


FIGURE 61

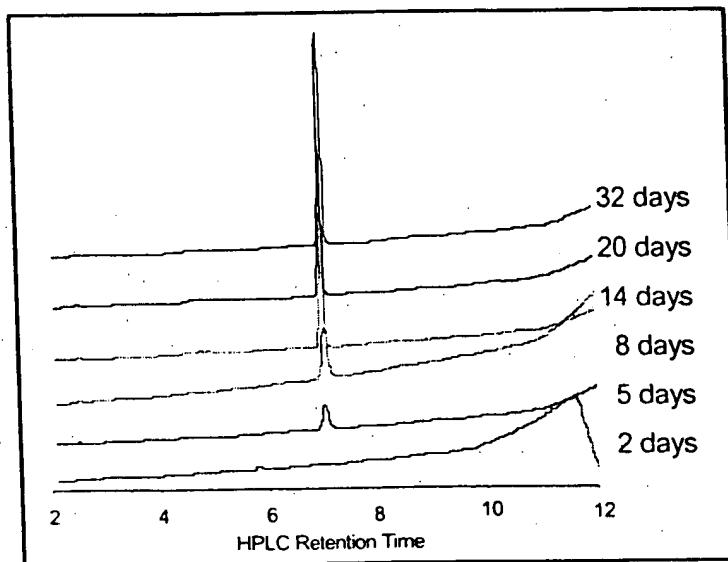


FIGURE 62

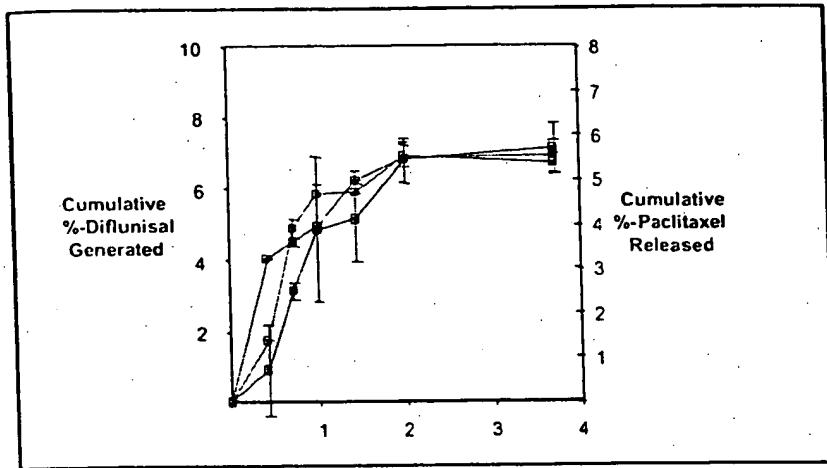


FIGURE 63

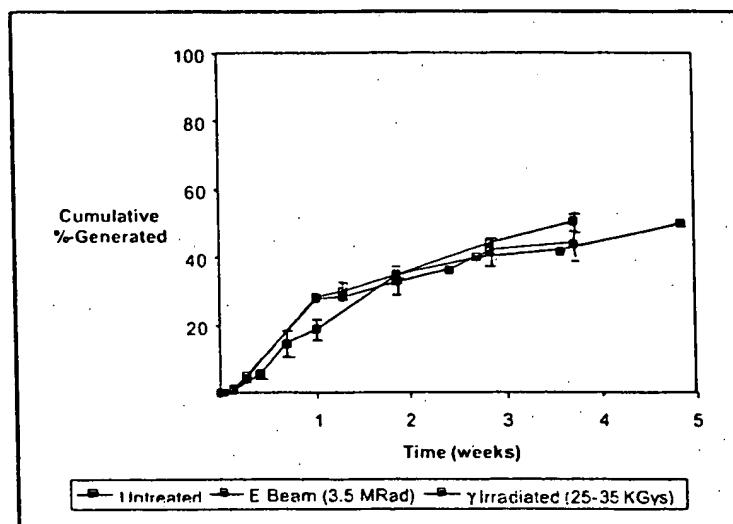


FIGURE 64

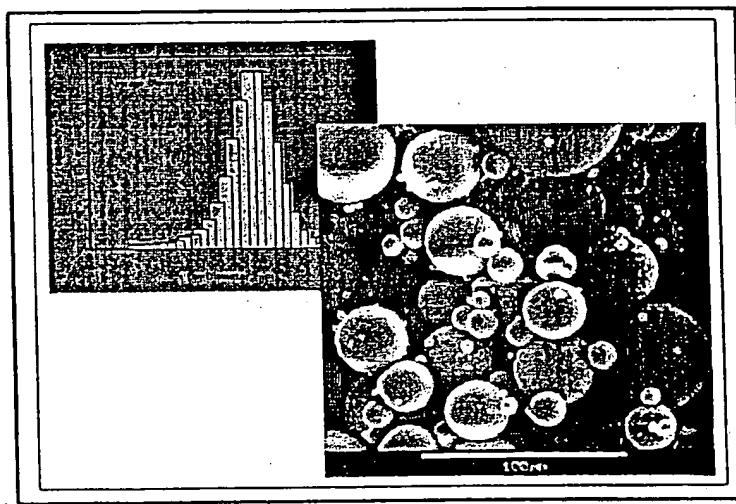


FIGURE 65

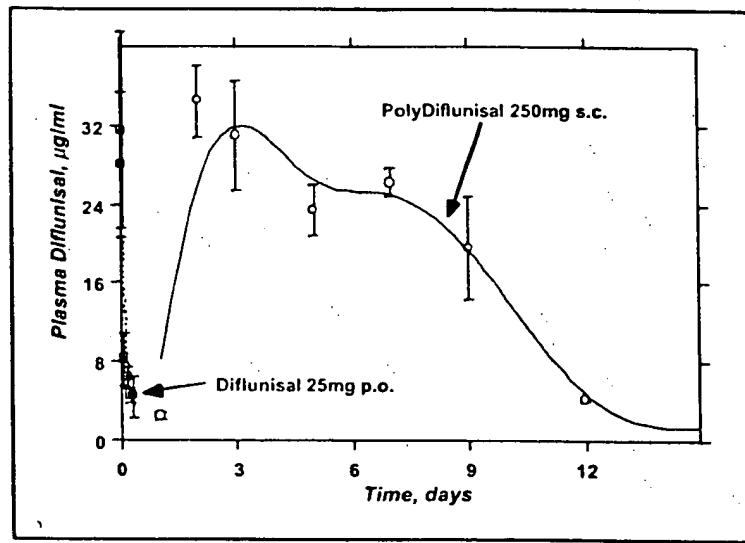


FIGURE 66

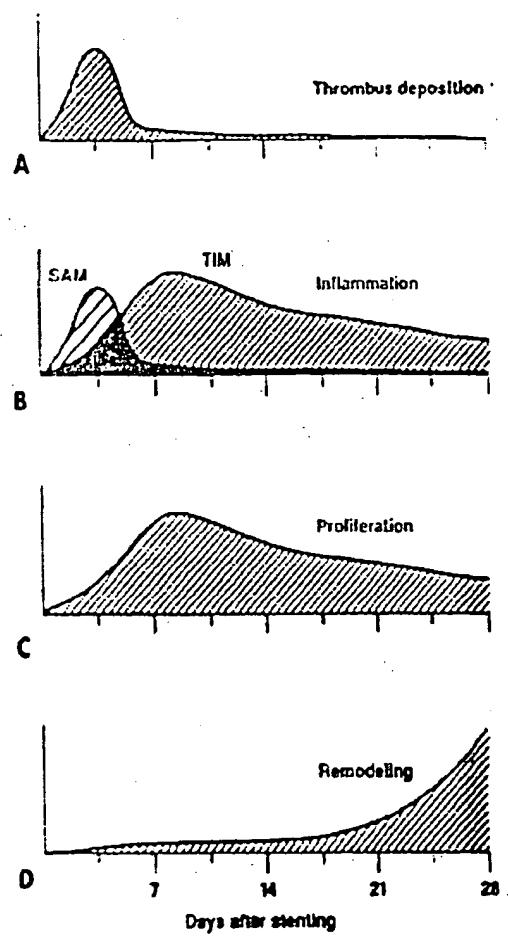


FIGURE 67

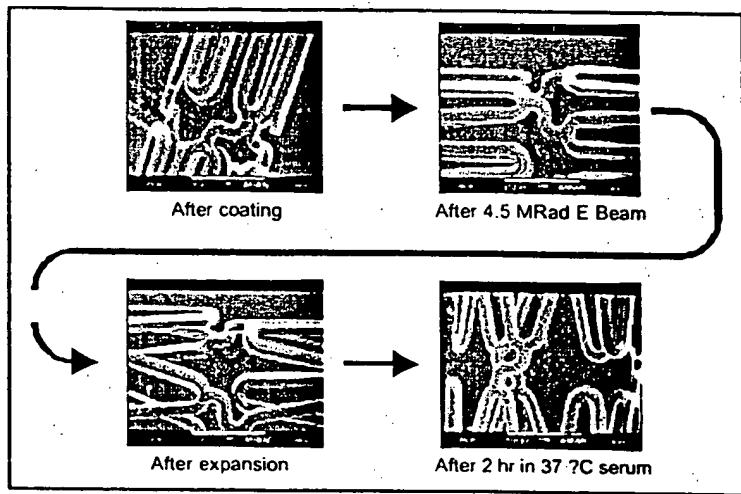


FIGURE 68

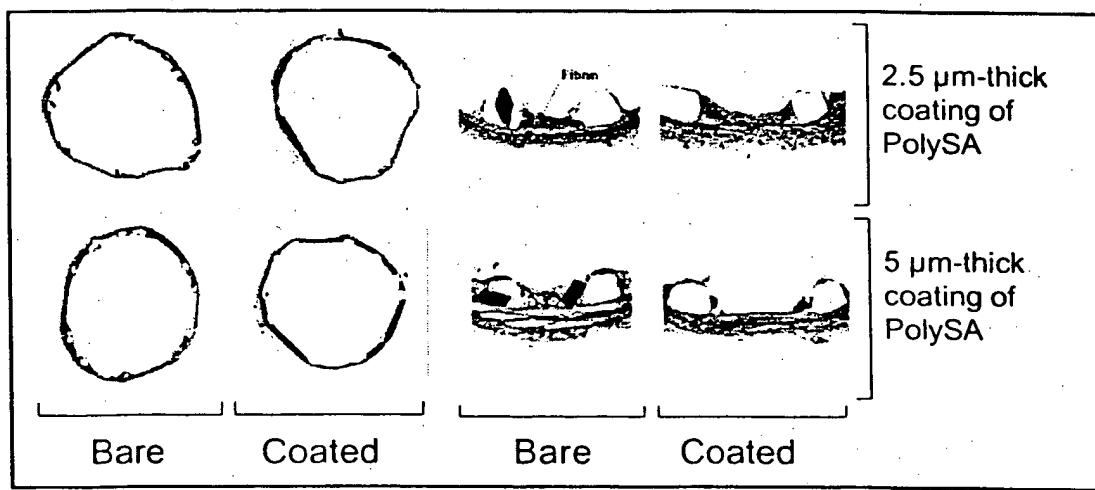


FIGURE 69

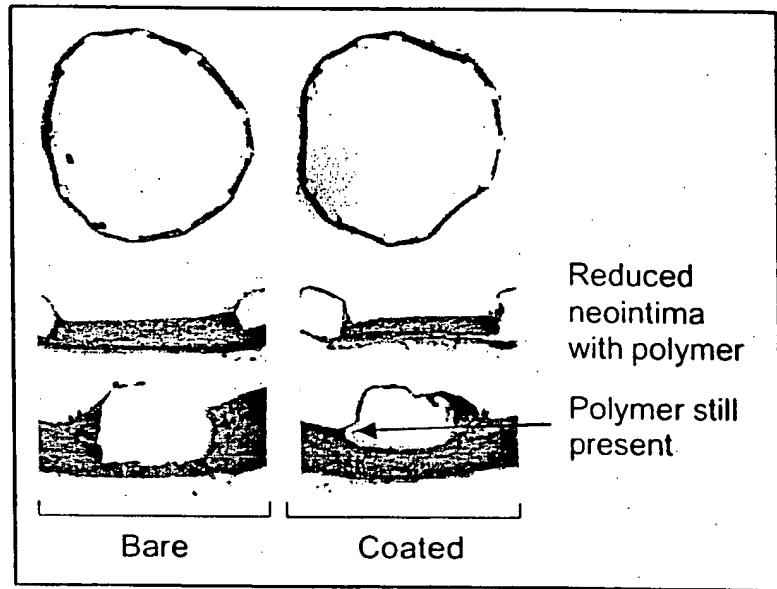


FIGURE 70

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